

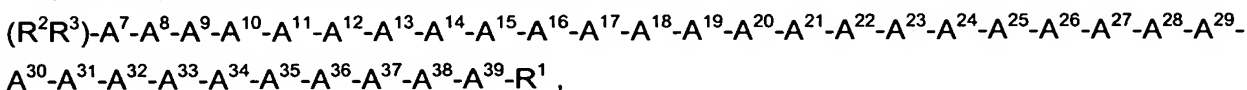
## IN THE CLAIMS

### **COMPLETE LISTING OF ALL CLAIMS, WITH MARKINGS AND STATUS IDENTIFIERS** (Currently amended claims showing deletions by ~~striketrough~~ and additions by underlining)

This listing of claims will replace all prior versions and listings of the claims in the application.

#### Listing of Claims:

1. (currently amended) A compound of formula (I),



(I)

wherein

A<sup>7</sup> is L-His, Ura, Paa, Pta, Amp, Tma-His, des-amino-His, or deleted;

A<sup>8</sup> is Ala,  $\beta$ -Ala, Gly, Ser, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala or N-Me-Gly;

A<sup>9</sup> is Glu, N-Me-Glu, N-Me-Asp or Asp;

A<sup>10</sup> is Gly, Acc,  $\beta$ -Ala or Aib;

A<sup>11</sup> is Thr or Ser;

A<sup>12</sup> is Phe, Acc, Aic, Aib, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal, Cha, Trp or (X<sup>6</sup>,X<sup>7</sup>,X<sup>8</sup>,X<sup>9</sup>,X<sup>10</sup>)Phe;

A<sup>13</sup> is Thr or Ser;

A<sup>14</sup> is Ser or Aib;

A<sup>15</sup> is Asp or Glu;

A<sup>16</sup> is Val, Acc, Aib, Leu, Ile, Tle, Nle, Abu, Ala or Cha;

A<sup>17</sup> is Ser, Aib or Thr;

A<sup>18</sup> is Ser, Lys or Thr;

A<sup>19</sup> is Tyr, Cha, Phe, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal, Acc or (X<sup>6</sup>,X<sup>7</sup>,X<sup>8</sup>,X<sup>9</sup>,X<sup>10</sup>)Phe;

A<sup>20</sup> is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Val, Phe or (X<sup>6</sup>,X<sup>7</sup>,X<sup>8</sup>,X<sup>9</sup>,X<sup>10</sup>)Phe;

A<sup>21</sup> is Glu or Asp;

A<sup>22</sup> is Gly, Acc,  $\beta$ -Ala, Glu or Aib;

A<sup>23</sup> is Gln, Asp, Asn or Glu;

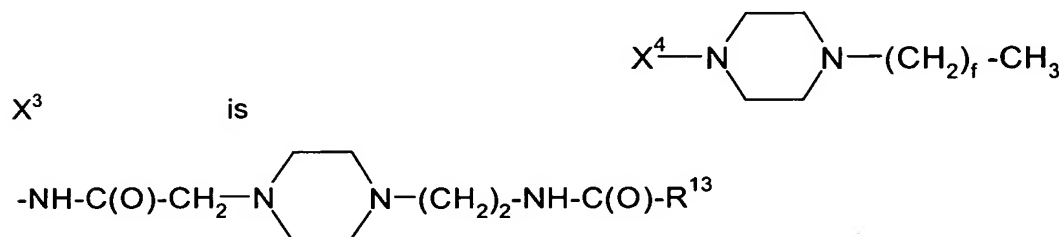
A<sup>24</sup> is Ala, Aib, Val, Abu, Tle or Acc;

A<sup>25</sup> is Ala, Aib, Val, Abu, Tle, Acc, Lys, Arg, hArg, Orn, HN-CH((CH<sub>2</sub>)<sub>n</sub>-N(R<sup>10</sup>R<sup>11</sup>))-C(O) or HN-CH((CH<sub>2</sub>)<sub>e</sub>-X<sup>3</sup>)-C(O);

A<sup>26</sup> is Lys, Arg, hArg, Orn, Lys(N<sup>E</sup>-decanoyl), HN-CH((CH<sub>2</sub>)<sub>n</sub>-N(R<sup>10</sup>R<sup>11</sup>))-C(O) or HN-CH((CH<sub>2</sub>)<sub>e</sub>-X<sup>3</sup>)-C(O);

A<sup>27</sup> is Glu, Asp, Leu, Aib or Lys;

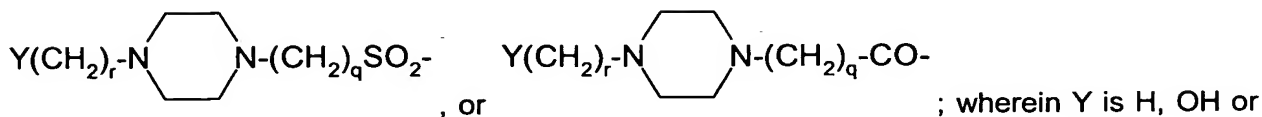
$A^{28}$  is Phe, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal,  $(X^6, X^7, X^8, X^9, X^{10})$ Phe, Aic, Acc, Aib, Cha or Trp;  
 $A^{29}$  is Ile, Acc, Aib, Leu, Nle, Cha, Tle, Val, Abu, Ala or Phe;  
 $A^{30}$  is Ala, Aib or Acc;  
 $A^{31}$  is Trp, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal, Phe, Acc, Aib,  $(X^6, X^7, X^8, X^9, X^{10})$ Phe or Cha;  
 $A^{32}$  is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Phe,  $(X^6, X^7, X^8, X^9, X^{10})$ Phe or Ala;  
 $A^{33}$  is Val, Acc, Aib, Leu, Ile, Tle, Nle, Cha, Ala, Phe, Abu, Lys or  $(X^6, X^7, X^8, X^9, X^{10})$ Phe;  
 $A^{34}$  is Lys, Arg, hArg, Orn,  $\text{HN-CH}((\text{CH}_2)_n\text{-N}(\text{R}^{10}\text{R}^{11}))\text{-C(O)}$  or  $\text{HN-CH}((\text{CH}_2)_e\text{-X}^3)\text{-C(O)}$ ;  
 $A^{35}$  is  $\beta$ -Ala, D-Ala, Gaba, Ava,  $\text{HN-}(\text{CH}_2)_m\text{-C(O)}$ , Aib, Acc, D-Arg or a D-amino acid;  
 $A^{36}$  is L- or D-Arg, D- or L-Lys, or Lys( $\text{N}^{\epsilon}$ -decanoyl) or Lys( $\text{N}^{\epsilon}$ -dodecanoyl) or D- or L-hArg, D- or L-Orn or  $\text{HN-CH}((\text{CH}_2)_n\text{-N}(\text{R}^{10}\text{R}^{11}))\text{-C(O)}$ , or  $\text{HN-CH}((\text{CH}_2)_e\text{-X}^3)\text{-C(O)}$ ;  
 ~~$A^{37}$  is Gly,  $\beta$ -Ala, Gaba, Aib, Acc, Act, Apc, Aun, Ava, Pro, Dhp, Dmt, Pip, 3-Hpr, 4-Hpr, L- or~~  
 $A^{37}$  is Gly,  $\beta$ -Ala, Gaba, Aib, Acc, Act, Apc, Aun, Ava, Pro, Dhp, Dmt, Pip, L- or  
D- Arg, L- or D- Asp or Glu, Lys( $\text{N}^{\epsilon}$ -decanoyl), Lys( $\text{N}^{\epsilon}$ -dodecanoyl), Lys( $\text{N}^{\epsilon}$ -octanoyl),  
Lys( $\text{N}^{\epsilon}$ -tetradecanoyl), or Ser( $\text{O}$ -decanoyl);  
 $A^{38}$  is D- or L- His, L- or D-Ala, Asn, Gln, Ser, Thr, Acc, Ado, Aib, Apc, Act, Arg, Ava, Gly,  $\beta$ -Ala, Gaba, or  $\text{HN-}(\text{CH}_2)_s\text{-C(O)}$ ;  
 $A^{39}$  is D- or L- His, L- or D-Ala, Asn, Gln, Ser, Thr, Acc, Ado, Aib, Apc, Act, Arg, Aun, Gly,  $\beta$ -Ala, Gaba, Lys( $\text{N}^{\epsilon}$ -octanoyl),  $\text{HN-}(\text{CH}_2)_s\text{-C(O)}$ , or deleted;  
 $\text{R}^1$  is OH,  $\text{NH}_2$ ;  $(\text{C}_1\text{-C}_{30})$ alkoxy, or  $\text{NH-X}^2\text{-CH}_2\text{-Z}^0$ , wherein  $\text{X}^2$  is a  $(\text{C}_0\text{-C}_2)$ ,  $(\text{C}_4\text{-C}_9)$  or  $(\text{C}_{11}\text{-C}_{19})$ hydrocarbon moiety and  $\text{Z}^0$  is H, OH,  $\text{CO}_2\text{H}$  or  $\text{CONH}_2$ ;



or  $\text{-C(O)-NHR}^{12}$ , wherein  $\text{X}^4$  is, independently for each occurrence,  $\text{-C(O)-}$ ,  $\text{-NH-C(O)-}$  or  $\text{-CH}_2\text{-}$ , and wherein  $f$  is, independently for each occurrence, an integer from 1 to 29 inclusive; each of  $\text{R}^2$  and  $\text{R}^3$  is independently selected from the group consisting of H,  $(\text{C}_1\text{-C}_{30})$ alkyl,  $(\text{C}_2\text{-C}_{30})$ alkenyl, optionally substituted phenyl $(\text{C}_1\text{-C}_{30})$ alkyl, optionally substituted naphthyl $(\text{C}_1\text{-C}_{30})$ alkyl, hydroxy $(\text{C}_1\text{-C}_{30})$ alkyl, hydroxy $(\text{C}_2\text{-C}_{30})$ alkenyl, hydroxyphenyl $(\text{C}_1\text{-C}_{30})$ alkyl, and hydroxynaphthyl $(\text{C}_1\text{-C}_{30})$ alkyl;

wherein the phenyl group of said optionally substituted phenyl $(\text{C}_1\text{-C}_{30})$ alkyl moiety, and said naphthyl group of said optionally substituted naphthyl $(\text{C}_1\text{-C}_{30})$ alkyl moiety each is, independently for each occurrence, substituted with 1 or more substituents selected, independently for each occurrence, from the group consisting of halo, OH,  $\text{NH}_2$ ,  $\text{NO}_2$  and CN;

or one of R<sup>2</sup> and R<sup>3</sup> is  $(\text{CH}_3)_2\text{-N}-\overset{\uparrow}{\text{C}}^+=\text{N}(\text{CH}_3)_2$ , (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>1</sub>-C<sub>30</sub>)alkylsulfonyl, C(O)X<sup>5</sup>,



; wherein Y is H, OH or NH<sub>2</sub>; r is 0 to 4; q is 0 to 4; and X<sup>5</sup> is (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>2</sub>-C<sub>30</sub>)alkenyl, phenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, naphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>2</sub>-C<sub>30</sub>)alkenyl, hydroxyphenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl or hydroxynaphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl;

X<sup>6</sup>, X<sup>7</sup>, X<sup>8</sup>, X<sup>9</sup>, X<sup>10</sup> for each occurrence is independently selected from the group consisting of H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, OH, OR<sup>4</sup>, NO<sub>2</sub>, CN, and halo;

R<sup>4</sup> is (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>2</sub>-C<sub>30</sub>)alkenyl, phenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, naphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>2</sub>-C<sub>30</sub>)alkenyl, hydroxyphenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl or hydroxynaphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl;

e is, independently for each occurrence, an integer from 1 to 4 inclusive;

m is, independently for each occurrence, an integer from 5 to 24 inclusive;

s is, independently for each occurrence, an integer from 5 to 10 or from 12 to 20 inclusive;

n is, independently for each occurrence, an integer from 1 to 5, inclusive;

each of R<sup>10</sup> and R<sup>11</sup> is, independently for each occurrence, H, (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>1</sub>-



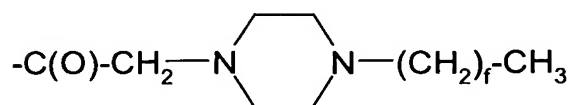
(C<sub>30</sub>)alkylsulfonyl, -C((NH)(NH<sub>2</sub>)) or ; and

R<sup>12</sup> and R<sup>13</sup> each is, independently for each occurrence, (C<sub>1</sub>-C<sub>30</sub>)alkyl;

provided that:

when A<sup>7</sup> is Ura, Paa or Pta, then R<sup>2</sup> and R<sup>3</sup> are deleted;

when R<sup>10</sup> is (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>1</sub>-C<sub>30</sub>)alkylsulfonyl, -C((NH)(NH<sub>2</sub>)) or



, then R<sup>11</sup> is H or (C<sub>1</sub>-C<sub>30</sub>)alkyl;

(i) at least one amino acid of a compound of formula (I) is not the same as the native sequence of hGLP-1(7-38 or -39)NH<sub>2</sub> or hGLP-1(7-38 or -39)OH;

(ii) a compound of formula (I) is not an analogue of hGLP-1(7-38 or -39)NH<sub>2</sub> or hGLP-1(7-38, or -39)OH wherein a single position has been substituted by Ala;

(iii) a compound of formula (I) is not (Arg<sup>26,34</sup>, Lys<sup>38</sup>)hGLP-1(7-38)-E, (Lys<sup>26</sup>(N<sup>ε</sup>-alkanoyl))hGLP-1(7-38)-E, (Lys<sup>34</sup>(N<sup>ε</sup>-alkanoyl))hGLP-1(7-38)-E, (Lys<sup>26,34</sup>-bis(N<sup>ε</sup>-

alkanoyl))hGLP-1(7-38)-E, (Arg<sup>26</sup>, Lys<sup>34</sup>(N<sup>c</sup>-alkanoyl))hGLP-1(8-38)-E, (Arg<sup>26,34</sup>, Lys<sup>36</sup>(N<sup>c</sup>-alkanoyl))hGLP-1(7-38)-E or (Arg<sup>26,34</sup>, Lys<sup>38</sup>(N<sup>c</sup>-alkanoyl))hGLP-1(7-38)-E, wherein E is -OH or -NH<sub>2</sub>;

(iv) a compound of formula (I) is not Z<sup>1</sup>-hGLP-1(7-38)-OH, Z<sup>1</sup>-hGLP-1(7-38)-NH<sub>2</sub>; wherein Z<sup>1</sup> is selected from the group consisting of:

(a) (Arg<sup>26</sup>), (Arg<sup>34</sup>), (Arg<sup>26,34</sup>), (Lys<sup>36</sup>), (Arg<sup>26</sup>, Lys<sup>36</sup>), (Arg<sup>34</sup>, Lys<sup>36</sup>), (D-Lys<sup>36</sup>), (Arg<sup>36</sup>), (D-Arg<sup>36</sup>), (Arg<sup>26,34</sup>, Lys<sup>36</sup>) or (Arg<sup>26,36</sup>, Lys<sup>34</sup>);

(b) (Asp<sup>21</sup>);

(c) at least one of (Aib<sup>8</sup>), (D-Ala<sup>8</sup>) and (Asp<sup>9</sup>); and

(d) (Tyr<sup>7</sup>), (N-acyl-His<sup>7</sup>), (N-alkyl-His<sup>7</sup>), (N-acyl-D-His<sup>7</sup>) or (N-alkyl-D-His<sup>7</sup>); and

(v) a compound of formula (I) is not a combination of any two of the substitutions listed in groups (a) to (d);

or a pharmaceutically acceptable salt thereof.

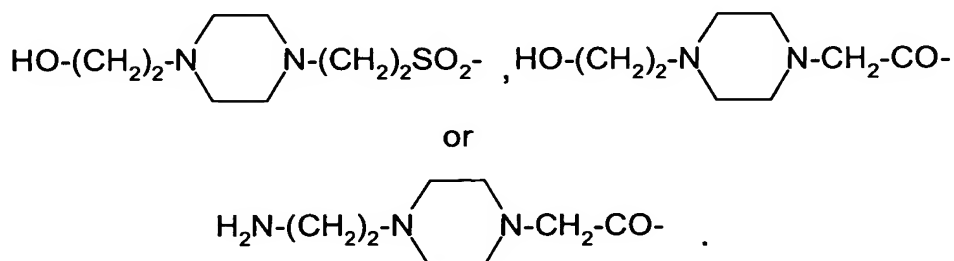
2. (original) A compound according to claim 1, wherein A<sup>11</sup> is Thr; A<sup>13</sup> is Thr; A<sup>15</sup> is Asp; A<sup>17</sup> is Ser; A<sup>18</sup> is Ser or Lys; A<sup>21</sup> is Glu; A<sup>23</sup> is Gln or Glu; A<sup>27</sup> is Glu, Leu, Aib or Lys; and A<sup>31</sup> is Trp, Phe, 1Nal or 2Nal; or a pharmaceutically acceptable salt thereof.

3. (original) A compound according to claim 2, wherein A<sup>9</sup> is Glu, N-Me-Glu or N-Me-Asp; A<sup>12</sup> is Phe, Acc, 1Nal, 2Nal, or Aic; A<sup>16</sup> is Val, Acc or Aib; A<sup>19</sup> is Tyr, 1Nal or 2Nal; A<sup>20</sup> is Leu, Acc or Cha; A<sup>24</sup> is Ala, Aib or Acc; A<sup>25</sup> is Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH((CH<sub>2</sub>)<sub>n</sub>-N(R<sup>10</sup>R<sup>11</sup>))-C(O) or HN-CH((CH<sub>2</sub>)<sub>e</sub>-X<sup>3</sup>)-C(O); A<sup>28</sup> is Phe, 1Nal or 2Nal; A<sup>29</sup> is Ile or Acc; A<sup>30</sup> is Ala or Aib; A<sup>32</sup> is Leu, Acc or Cha; and A<sup>33</sup> is Val, Lys or Acc; or a pharmaceutically acceptable salt thereof.

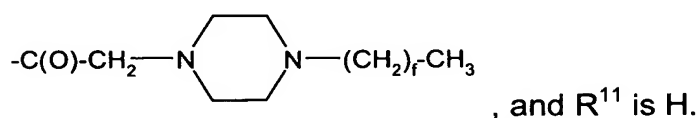
4. (original) A compound according to claim 1, wherein A<sup>8</sup> is Ala, Gly, Ser, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A<sup>10</sup> is Gly; A<sup>12</sup> is Phe, 1Nal, 2Nal, A6c or A5c; A<sup>16</sup> is Val, A6c or A5c; A<sup>20</sup> is Leu, A6c, A5c or Cha; A<sup>22</sup> is Gly, β-Ala, Glu or Aib; A<sup>24</sup> is Ala or Aib; A<sup>29</sup> is Ile, A6c or A5c; A<sup>32</sup> is Leu, A6c, A5c or Cha; A<sup>33</sup> is Val, Lys, A6c or A5c; A<sup>35</sup> is Aib, β-Ala, Ado, A6c, A5c, D-Arg or Acc; A<sup>37</sup> is Gly, Aib, β-Ala, D-Ala, Pro, Asp, Aun or D-Asp; A<sup>38</sup> is D- or L- His, Asn, Ser, Apc, Act, Gly, β-Ala or Gaba; and A<sup>39</sup> is Ser, Thr or Aib; or a pharmaceutically acceptable salt thereof.

5. (original) A compound according to claim 4 or a pharmaceutically acceptable salt thereof, X<sup>4</sup> for each occurrence is -C(O)-; and R<sup>1</sup> is OH or NH<sub>2</sub>; or a pharmaceutically acceptable salt thereof.

6. (original) A compound according to claim 5 or a pharmaceutically acceptable salt thereof, wherein  $R^2$  is H and  $R^3$  is  $(C_1-C_{30})$ alkyl,  $(C_2-C_{30})$ alkenyl,  $(C_1-C_{30})$ acyl,  $(C_1-C_{30})$ alkylsulfonyl,



7. (original) A compound according to claim 5 or a pharmaceutically acceptable salt thereof, wherein  $R^{10}$  is  $(C_1-C_{30})$ acyl,  $(C_1-C_{30})$ alkylsulfonyl or

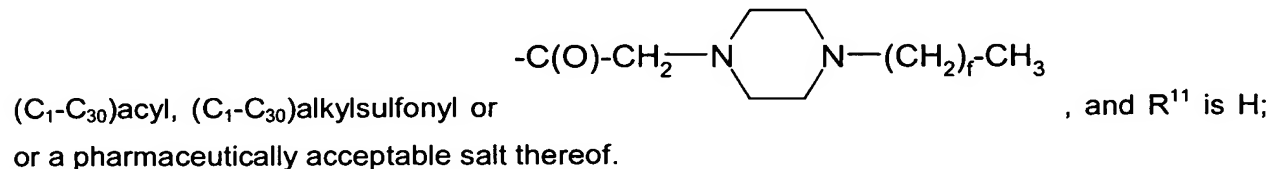


8. (original) A compound according to claim 7 or a pharmaceutically acceptable salt thereof, wherein  $R^{10}$  is  $(C_4-C_{20})$ acyl,  $(C_4-C_{20})$ alkylsulfonyl or

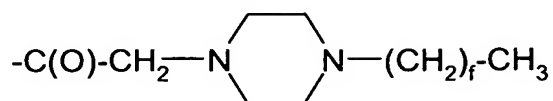


9. (original) A compound according to claim 1, wherein:

$A^8$  is Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly;  $A^{10}$  is Gly;  $A^{12}$  is Phe, 1Nal, 2Nal, A6c or A5c;  $A^{16}$  is Val, A6c or A5c;  $A^{20}$  is Leu, A6c, A5c or Cha;  $A^{22}$  is Gly,  $\beta$ -Ala, Glu or Aib;  $A^{24}$  is Ala or Aib;  $A^{29}$  is Ile, A6c or A5c;  $A^{32}$  is Leu, A6c, A5c or Cha;  $A^{33}$  is Val, Lys, A6c or A5c;  $A^{35}$  is Aib,  $\beta$ -Ala, Ado, A6c, A5c or D-Arg; and  $A^{37}$  is Gly, Aib,  $\beta$ -Ala, D-Ala, Pro or D-Asp;  $A^{38}$  is D- or L- His, Asn, Ser, Gly,  $\beta$ -Ala or Gaba; and  $A^{39}$  is Ser, or deleted;  $X^4$  for each occurrence is  $-\text{C}(\text{O})-$ ; e for each occurrence is independently 1 or 2;  $R^1$  is OH or  $\text{NH}_2$ ;  $R^{10}$  is



10. (original) A compound according to claim 9, wherein R<sup>10</sup> is (C<sub>4</sub>-C<sub>20</sub>)acyl, (C<sub>4</sub>-



C<sub>20</sub>)alkylsulfonyl or , or a pharmaceutically acceptable salt thereof.

11. (original) A compound according to claim 1 wherein said compound is according to the formula:

(Aib<sup>8,35</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, Pro<sup>37</sup>, Ser<sup>38, 39</sup>)hGLP-1(7-39)- NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, Asn<sup>38</sup>)hGLP-1(7-38)- NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, Ser<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Gaba<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, β-Ala<sup>37</sup>, His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, D-His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, β-Ala<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35</sup>, Arg<sup>26,34</sup>, β-Ala<sup>37</sup>, His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, Gly<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Gly<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, β-Ala<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Gaba<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>34</sup>, Phe<sup>31</sup>, His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, Gaba<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, Ava<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Ava<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>34</sup>, Phe<sup>31</sup>, D-His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>34</sup>, Phe<sup>31</sup>, Gly<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Gly<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, D-His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, β-Ala<sup>37</sup>, D-His<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, β-Ala<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35</sup>, Arg<sup>26,34</sup>, Phe<sup>31</sup>, β-Ala<sup>37,38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

(Aib<sup>8,35,37</sup>, Arg<sup>34</sup>, Phe<sup>31</sup>, β-Ala<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>; or

(Aib<sup>8,35,37</sup>, Arg<sup>34</sup>, Phe<sup>31</sup>, Gaba<sup>38</sup>)hGLP-1(7-38) NH<sub>2</sub>;

or a pharmaceutically acceptable salt thereof.

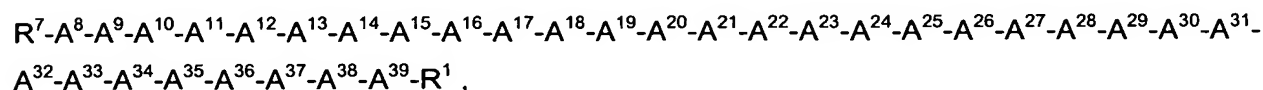
12. (original) A pharmaceutical composition comprising an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.

13. (original) A method of eliciting an agonist effect from a GLP-1 receptor in a subject in need thereof which comprises administering to said subject an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof.

14. (original) A method of treating a disease selected from the group consisting of Type I diabetes, Type II diabetes, obesity, glucagonomas, secretory disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system disease, restenosis, neurodegenerative disease, renal failure, congestive heart failure, nephrotic syndrome, cirrhosis, pulmonary edema, hypertension, treatment of respiratory distress, disorders wherein the reduction of food intake is desired, hypoglycemia and malabsorption syndrome associated with gastroectomy or small bowel resection, in a subject in need thereof which comprises administering to said subject an effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof.

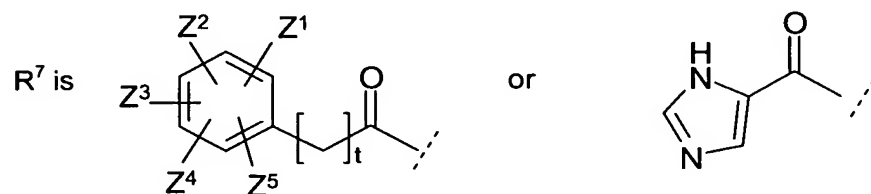
15. (original) A method according to claim 14 wherein said disease is Type I diabetes or Type II diabetes.

16. (currently amended) A compound of formula (II),



(II)

wherein



$A^8$  is Ala,  $\beta$ -Ala, Gly, Ser, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala or N-Me-Gly;

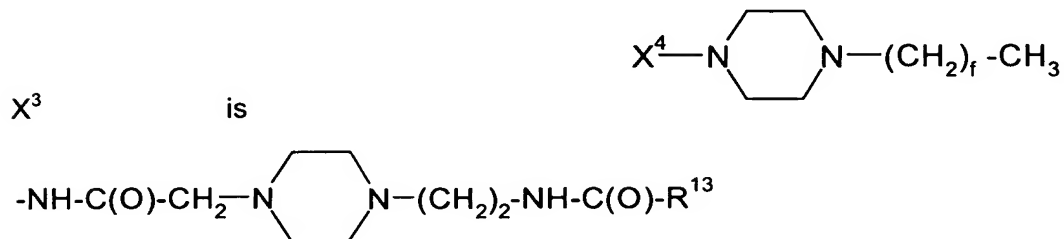
$A^9$  is Glu, N-Me-Glu, N-Me-Asp or Asp;

$A^{10}$  is Gly, Acc,  $\beta$ -Ala or Aib;  
 $A^{11}$  is Thr or Ser;  
 $A^{12}$  is Phe, Acc, Aic, Aib, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal, Cha, Trp or  $(X^6, X^7, X^8, X^9, X^{10})$ Phe;  
 $A^{13}$  is Thr or Ser;  
 $A^{14}$  is Ser or Aib;  
 $A^{15}$  is Asp or Glu;  
 $A^{16}$  is Val, Acc, Aib, Leu, Ile, Tle, Nle, Abu, Ala or Cha;  
 $A^{17}$  is Ser, Aib or Thr;  
 $A^{18}$  is Ser, Lys or Thr;  
 $A^{19}$  is Tyr, Cha, Phe, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal, Acc or  $(X^6, X^7, X^8, X^9, X^{10})$ Phe;  
 $A^{20}$  is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Val, Phe or  $(X^6, X^7, X^8, X^9, X^{10})$ Phe;  
 $A^{21}$  is Glu or Asp;  
 $A^{22}$  is Gly, Acc,  $\beta$ -Ala, Glu or Aib;  
 $A^{23}$  is Gln, Asp, Asn or Glu;  
 $A^{24}$  is Ala, Aib, Val, Abu, Tle or Acc;  
 $A^{25}$  is Ala, Aib, Val, Abu, Tle, Acc, Lys, Arg, hArg, Orn,  $\text{HN-CH}((\text{CH}_2)_n\text{-N(R}^{10}\text{R}^{11}))\text{-C(O)}$  or  $\text{HN-CH}((\text{CH}_2)_e\text{-X}^3)\text{-C(O)}$ ;  
 $A^{26}$  is Lys, Arg, hArg, Orn,  $\text{Lys(N}^{\text{E}}\text{-decanoyl)}$ ,  $\text{HN-CH}((\text{CH}_2)_n\text{-N(R}^{10}\text{R}^{11}))\text{-C(O)}$  or  $\text{HN-CH}((\text{CH}_2)_e\text{-X}^3)\text{-C(O)}$ ;  
 $A^{27}$  is Glu Asp, Leu, Aib or Lys;  
 $A^{28}$  is Phe, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal,  $(X^6, X^7, X^8, X^9, X^{10})$ Phe, Aic, Acc, Aib, Cha or Trp;  
 $A^{29}$  is Ile, Acc, Aib, Leu, Nle, Cha, Tle, Val, Abu, Ala or Phe;  
 $A^{30}$  is Ala, Aib or Acc;  
 $A^{31}$  is Trp, 2-Pal, 3-Pal, 4-Pal, 1Nal, 2Nal, Phe, Acc, Aib,  $(X^6, X^7, X^8, X^9, X^{10})$ Phe or Cha;  
 $A^{32}$  is Leu, Acc, Aib, Nle, Ile, Cha, Tle, Phe,  $(X^6, X^7, X^8, X^9, X^{10})$ Phe or Ala;  
 $A^{33}$  is Val, Acc, Aib, Leu, Ile, Tle, Nle, Cha, Ala, Phe, Abu, Lys or  $(X^6, X^7, X^8, X^9, X^{10})$ Phe;  
 $A^{34}$  is Lys, Arg, hArg, Orn,  $\text{HN-CH}((\text{CH}_2)_n\text{-N(R}^{10}\text{R}^{11}))\text{-C(O)}$  or  $\text{HN-CH}((\text{CH}_2)_e\text{-X}^3)\text{-C(O)}$ ;  
 $A^{35}$  is  $\beta$ -Ala, D-Ala, Gaba, Ava,  $\text{HN-(CH}_2)_m\text{-C(O)}$ , Aib, Acc, D-Arg, a D-amino acid or deleted;  
 $A^{36}$  is L- or D-Arg, D- or L-Lys, or  $\text{Lys(N}^{\text{E}}\text{-decanoyl)}$  or  $\text{Lys(N}^{\text{E}}\text{-dodecanoyl)}$  or D- or L-hArg, D- or L-Orn or  $\text{HN-CH}((\text{CH}_2)_n\text{-N(R}^{10}\text{R}^{11}))\text{-C(O)}$ ,  $\text{HN-CH}((\text{CH}_2)_e\text{-X}^3)\text{-C(O)}$ , or deleted;  
 ~~$A^{37}$  is Gly,  $\beta$ -Ala, Gaba, Aib, Acc, Act, Apc, Aun, Ava, Pro, Dhp, Dmt, Pip, 3-Hpr, 4-Hpr, L- or~~  
 $A^{37}$  is Gly,  $\beta$ -Ala, Gaba, Aib, Acc, Act, Apc, Aun, Ava, Pro, Dhp, Dmt, Pip, L- or  
D- Arg, L- or D- Asp or Glu,  $\text{Lys(N}^{\text{E}}\text{-decanoyl)}$ ,  $\text{Lys(N}^{\text{E}}\text{-dodecanoyl)}$ ,  $\text{Lys(N}^{\text{E}}\text{-octanoyl)}$ ,  $\text{Lys(N}^{\text{E}}\text{-tetradecanoyl)}$ ,  $\text{Ser(O-decanoyl)}$ , or deleted;  
 $A^{38}$  is D- or L- His, L- or D-Ala, Asn, Gln, Ser, Thr, Acc, Ado, Aib, Apc, Act, Arg, Ava, Gly,  $\beta$ -Ala, Gaba,  $\text{HN-(CH}_2)_s\text{-C(O)}$   $\text{HN-(CH}_2)_m\text{-C(O)}$ , or deleted;



A<sup>39</sup> is D- or L- His, L- or D-Ala, Asn, Gln, Ser, Thr, Acc, Ado, Aib, Apc, Act, Arg, Aun, Gly,  $\beta$ -Ala, Gaba, Lys(N<sup>e</sup>-octanoyl),  $\text{HN}-(\text{CH}_2)_s-\text{C}(\text{O})$   $\text{HN}-(\text{CH}_2)_m-\text{C}(\text{O})$ , or deleted;

R<sup>1</sup> is OH, NH<sub>2</sub>; (C<sub>1</sub>-C<sub>30</sub>)alkoxy, or NH-X<sup>2</sup>-CH<sub>2</sub>-Z<sup>0</sup>, wherein X<sup>2</sup> is a (C<sub>0</sub>-C<sub>20</sub>)hydrocarbon moiety and Z<sup>0</sup> is H, OH, CO<sub>2</sub>H or CONH<sub>2</sub>;



or -C(O)-NHR<sup>12</sup>, wherein X<sup>4</sup> is, independently for each occurrence, -C(O)-, -NH-C(O)- or -CH<sub>2</sub>-, and wherein f is, independently for each occurrence, an integer from 1 to 29 inclusive; X<sup>6</sup>, X<sup>7</sup>, X<sup>8</sup>, X<sup>9</sup>, X<sup>10</sup> for each occurrence is independently selected from the group consisting of H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, OH, OR<sup>4</sup>, NO<sub>2</sub>, CN, and halo;

R<sup>4</sup> is (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>2</sub>-C<sub>30</sub>)alkenyl, phenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, naphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>2</sub>-C<sub>30</sub>)alkenyl, hydroxyphenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl or hydroxynaphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl; Z<sup>1</sup>, Z<sup>2</sup>, Z<sup>3</sup>, Z<sup>4</sup>, Z<sup>5</sup> for each occurrence is independently selected from the group consisting of H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, OH, OR<sup>4</sup>, NO<sub>2</sub>, CN, and halo; ~~Z<sup>1</sup> and Z<sup>2</sup> can joint together to form a ring system;~~ (C<sub>1</sub>-C<sub>6</sub>)alkyl, OH, OR<sup>4</sup>, NO<sub>2</sub>, CN, and halo; Z<sup>1</sup> and Z<sup>2</sup> can join together to form a ring system;

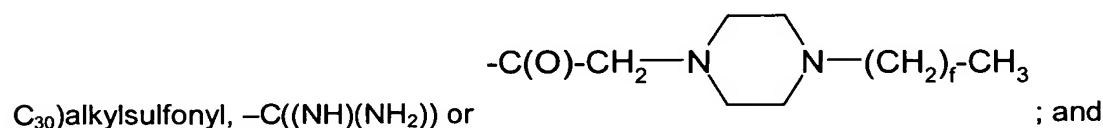
e is, independently for each occurrence, an integer from 1 to 4 inclusive;

m is, independently for each occurrence, an integer from 5 to 24 inclusive;

n is, independently for each occurrence, an integer from 1 to 5, inclusive;

t is, independently for each occurrence, an integer from 0 to 4, inclusive;

each of R<sup>10</sup> and R<sup>11</sup> is, independently for each occurrence, H, (C<sub>1</sub>-C<sub>30</sub>)alkyl, (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>1</sub>-

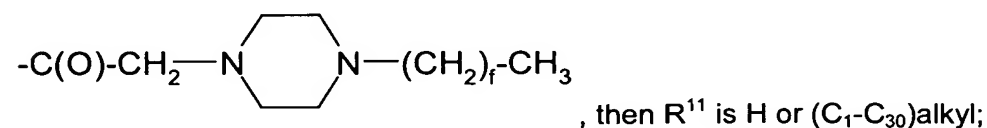


R<sup>12</sup> and R<sup>13</sup> each is, independently for each occurrence, (C<sub>1</sub>-C<sub>30</sub>)alkyl;

provided that:

R<sup>7</sup> is not C(O)X<sup>11</sup>, wherein X<sup>11</sup> is phenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, naphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>1</sub>-C<sub>30</sub>)alkyl, hydroxy(C<sub>2</sub>-C<sub>30</sub>)alkenyl, hydroxyphenyl(C<sub>1</sub>-C<sub>30</sub>)alkyl or hydroxynaphthyl(C<sub>1</sub>-C<sub>30</sub>)alkyl;

when R<sup>10</sup> is (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>1</sub>-C<sub>30</sub>)alkylsulfonyl, -C((NH)(NH<sub>2</sub>)) or



or a pharmaceutically acceptable salt thereof.

17. (original) A compound according to claim 16, wherein A<sup>11</sup> is Thr; A<sup>13</sup> is Thr; A<sup>15</sup> is Asp; A<sup>17</sup> is Ser; A<sup>18</sup> is Ser or Lys; A<sup>21</sup> is Glu; A<sup>23</sup> is Gln or Glu; A<sup>27</sup> is Glu, Leu, Aib or Lys; and A<sup>31</sup> is Trp, Phe, 1Nal or 2Nal; or a pharmaceutically acceptable salt thereof.

18. (original) A compound according to claim 17, A<sup>7</sup> is 4-imidazol-carbonyl, 4-nitrophenyl-acetyl, 3-chloro-4-hydroxyphenyl-acetyl, 4-hydroxyphenyl-acetyl, 3-(4-aminophenyl)-propionyl, 3-(4-nitrophenyl)-propionyl, 3-(3,4-difluorophenyl)-propionyl, 3-fluoro-4-hydroxyphenyl-acetyl or 4-aminophenyl-acetyl; A<sup>9</sup> is Glu, N-Me-Glu or N-Me-Asp; A<sup>12</sup> is Phe, Acc, 1Nal, 2Nal, or Aic; A<sup>16</sup> is Val, Acc or Aib; A<sup>19</sup> is Tyr, 1Nal or 2Nal; A<sup>20</sup> is Leu, Acc or Cha; A<sup>24</sup> is Ala, Aib or Acc; A<sup>25</sup> is Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH((CH<sub>2</sub>)<sub>n</sub>-N(R<sup>10</sup>R<sup>11</sup>))-C(O) or HN-CH((CH<sub>2</sub>)<sub>e</sub>-X<sup>3</sup>)-C(O); A<sup>28</sup> is Phe, 1Nal or 2Nal; A<sup>29</sup> is Ile or Acc; A<sup>30</sup> is Ala or Aib; A<sup>32</sup> is Leu, Acc or Cha; and A<sup>33</sup> is Val, Lys or Acc; or a pharmaceutically acceptable salt thereof.

19. (original) A compound according to claim 18, wherein A<sup>8</sup> is Ala, Gly, Ser, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A<sup>10</sup> is Gly; A<sup>12</sup> is Phe, 1Nal, 2Nal, A6c or A5c; A<sup>16</sup> is Val, A6c or A5c; A<sup>20</sup> is Leu, A6c, A5c or Cha; A<sup>22</sup> is Gly, β-Ala, Glu or Aib; A<sup>24</sup> is Ala or Aib; A<sup>29</sup> is Ile, A6c or A5c; A<sup>32</sup> is Leu, A6c, A5c or Cha; A<sup>33</sup> is Val, Lys, A6c or A5c; A<sup>35</sup> is Aib, β-Ala, Ado, A6c, A5c, D-Arg, Acc or Gly; A<sup>37</sup> is Gly, Aib, β-Ala, D-Ala, Pro, Asp, Aun or D-Asp; A<sup>38</sup> is D- or L- His, Asn, Ser, Apc, Act, Gly, β-Ala or Gaba; and A<sup>39</sup> is Ser, Thr or Aib; or a pharmaceutically acceptable salt thereof.

20. (original) A compound according to claim 19 or a pharmaceutically acceptable salt thereof, wherein X<sup>4</sup> for each occurrence is -C(O)-; and R<sup>1</sup> is OH or NH<sub>2</sub>; or a pharmaceutically acceptable salt thereof.

21. (original) A compound according to claim 16 wherein A<sup>8</sup> is Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala or N-Me-Gly; A<sup>10</sup> is Gly; A<sup>12</sup> is Phe, 1Nal, 2Nal, A6c or A5c; A<sup>16</sup> is Val, A6c or A5c; A<sup>20</sup> is Leu, A6c, A5c or Cha; A<sup>22</sup> is Gly, β-Ala, Glu or Aib; A<sup>24</sup> is Ala or Aib; A<sup>29</sup> is Ile, A6c or A5c; A<sup>32</sup> is Leu, A6c, A5c or Cha; A<sup>33</sup> is Val, Lys, A6c or A5c; A<sup>35</sup> is Aib, β-Ala, Ado, A6c, A5c D-Arg or Gly; and A<sup>37</sup> is Gly, Aib, β-Ala, D-Ala, Pro or D-Asp; A<sup>38</sup> is D- or L- His, Asn, Ser, Gly, β-Ala or Gaba; and A<sup>39</sup> is Ser, or deleted; X<sup>4</sup> for each occurrence is -C(O)-; e for each occurrence is independently 1 or 2; R<sup>1</sup> is OH or NH<sub>2</sub>; R<sup>10</sup> is (C<sub>1</sub>-C<sub>30</sub>)acyl, (C<sub>1</sub>-

$$-\text{C}(\text{O})-\text{CH}_2-\text{N} \begin{array}{c} \diagup \quad \diagdown \\ \text{---} \quad \text{---} \\ \diagdown \quad \diagup \end{array} \text{N}-(\text{CH}_2)_f-\text{CH}_3$$

$\text{C}_{30}$ )alkylsulfonyl or , and  $\text{R}^{11}$  is H; or a pharmaceutically acceptable salt thereof.

22. (original) A compound according to claim 21 wherein  $\text{R}^{10}$  is  $(\text{C}_4\text{-C}_{20})\text{acyl}$ ,  $(\text{C}_4\text{-C}_{20})\text{alkylsulfonyl}$  or , or a pharmaceutically acceptable salt thereof.

$$-\text{C}(\text{O})-\text{CH}_2-\text{N} \begin{array}{c} \diagup \quad \diagdown \\ \text{---} \quad \text{---} \\ \diagdown \quad \diagup \end{array} \text{N}-(\text{CH}_2)_f-\text{CH}_3$$

$\text{C}_{20}$ )alkylsulfonyl or , or a pharmaceutically acceptable salt thereof.

23. (original) A compound according to claim 16 wherein said compound is

$(4\text{Hppa}^7)\text{GLP-1(7-36)NH}_2$ ;

$(3\text{Hppa}^7)\text{GLP-1(7-36)NH}_2$ ;

$(\text{phenylacetyl}^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-fluoro-4-hydroxyphenyl-acetyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((4\text{-imidazol-carbonyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((4\text{-nitrophenyl-acetyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-chloro-4-hydroxyphenyl-acetyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((4\text{-hydroxyphenylacetyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((4\text{-aminophenyl-acetyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-}(3\text{-hydroxyphenyl})\text{-propionyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-phenyl-propionyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-}(4\text{-aminophenyl})\text{-propionyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-}(4\text{-nitrophenyl})\text{-propionyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-}(2\text{-hydroxyphenyl})\text{-propionyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

$((3\text{-}(3,4\text{-difluorophenyl})\text{-propionyl})^7)\text{hGLP-1(7-36)NH}_2$ ; or

$((3\text{-}(2,4\text{-dihydroxyphenyl})\text{-propionyl})^7)\text{hGLP-1(7-36)NH}_2$ ;

or a pharmaceutically acceptable salt thereof.

24. (original) A pharmaceutical composition comprising an effective amount of a compound according to claim 16 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.

25. (original) A method of eliciting an agonist effect from a GLP-1 receptor in a subject in need thereof which comprises administering to said subject an effective amount of a compound according to claim 16 or a pharmaceutically acceptable salt thereof.

26. (original) A method of treating a disease selected from the group consisting of Type I diabetes, Type II diabetes, obesity, glucagonomas, secretory disorders of the airway, metabolic disorder, arthritis, osteoporosis, central nervous system disease, restenosis, neurodegenerative disease, renal failure, congestive heart failure, nephrotic syndrome, cirrhosis, pulmonary edema, hypertension, treatment of respiratory distress, disorders wherein the reduction of food intake is desired, hypoglycemia and malabsorption syndrome associated with gastroectomy or small bowel resection, in a subject in need thereof which comprises administering to said subject an effective amount of a compound according to claim 16 or a pharmaceutically acceptable salt thereof.

27. (original) A method according to claim 26 wherein said disease is Type I diabetes or Type II diabetes.